11:45

MALIGNANT ARRHYTHMIAS AND "SILENT MYOCARDIAL ISCHEMIA" IN HYPERTENSIVE HEART DISEASE - PREVALENCE, VARIABILITY AND PROGNOSTIC RELEVANCE

Manfred Zehender, Thomas Meinertz, Stefan Kohlloser, Ursula Kasebeck, Charlotte Garisch, Hanjörg Just. Depart. of Cardiology, University of Freiburg, West Germany

Due to the increased risk of sudden death (SD) in pts with hypertensive heart disease (HHD), we prospectively studied 150 untreated pts with HHD (3 times >160/95 mmHg, mean: 173/98 mmHg, 112 men, 56±9 years, without evidence of coronary disease), for the prevalence, severity and interaction of ventricular arrhythmias (VA) and transient, asymptomatic ST-segment depression ST-D (>0.1mV, >1min) during 24h-Holter recording. 50 pts were then randomized to 4 weeks of placebo (P, 2x/die) and restudied to assess spontaneous variability (SV). Results: VA were present in 129/150 pts (86%, pairs:22 pts,tachycardia: 20 pts); prevalence was highest in 55 /150 pts with ST-D (p<0.05) and during episodes of ST-D (5.6 vs 0.5/min, p<0.001). Both parameters had similar day-night variations. A positive correlation was observed for total time of ST-D, Sokolow-Lyon Index and repetitive VA. After P, VA (-100%: 12% of pts, +>400%:17%), repetitive VA (-100% or first episode: 60%), but to a less extent ST-D showed a high SV. During a 3-year follow-up, D (10 pts), SD (5), myocardial infarction (6) were predictable by repetitive VA+ST-D.
Conclusions: Repetitive VA and silent ST-D are common and of prognostic relevance in pts with HHD. Therapeutic consequences, however, are limited by a marked day-night and day/day variability.

10:45

DEMONSTRATION OF A PRONOUNCED FORCE-FREQUENCY EFFECT DURING CATECHOLAMINE STIMULATION IN CONSCIOUS DOGS

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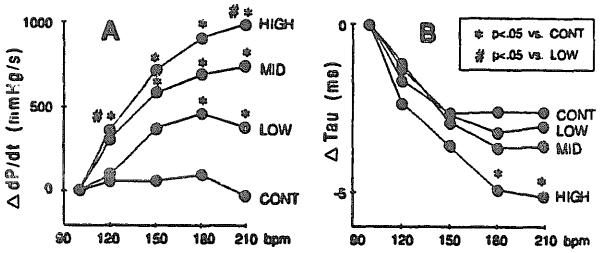
The effect of heart rate (HR) on contractility (force-frequency (FF) effect) is known to be small under basal condition in the intact heart, but such effects during stress are unknown. To assess such FF effects on contraction and relaxation, we examined 7 instrumented conscious dogs, in which HR could be controlled by atrial pacing after administration of a specific bradycardiac agent (UL-FS49, 0.5-0.75mg/kg). LV pressure (micromanometer) and wall thickness (WT:sonomicrometer) were measured under resting conditions and during dobutamine infusion at low, mid and high doses; 2.7, 5.4 and 10.7 μg/kg/min. At each dose, HR was progressively increased. LVEDP, LV peak pressure and end-diastolic WT were not significantly different at control and each level of HR at the three drug doses. Changes in peak LV (+) dP/dt (Figure A) and in time constant of LV pressure decay, Tau (Figure B) are plotted against HR.



These data show that a pronounced FF effect on LV contractility is evident during catecholamine stimulation. This effect was dose-dependent and increased LV relaxation was apparent only at the highest dose.

Tuesday, March 5, 1991
10:30AM-12:00NOON, Room 254, West Concourse
Myocardial Mechanics: Ischemia

10:30

EXTRACELLULAR MATRIX PROTEINS ARE A DETERMINANT OF LEFT VENTRICULAR DIASTOLIC ELASTANCE AT LOW FILLING PRESSURES

Richard A. Podolin, Lisa A. Brackman, James W. Covell, UCSD and San Diego VAMC, San Diego, California

We examined the contribution of the extracellular matrix proteins to left ventricular diastolic elastance (E) in isolated Sprague-Dawley rat hearts. Control (C) hearts (N=8) were perfused with a calcium free modified Krebs-Henseleit solution containing 2,3-butanedione 2-monoxime, a direct inhibitor of muscle contraction. A second group (DTNB)(N=5) was perfused with a similar solution, to which was added 1 mM 5,5'-Dithio(2-nitrobenzoic acid), a disulfide reagent which induces a collagenolytic reaction. Pressure-volume data were obtained by inflating a compliant intraventricular balloon before and after 3 hours of perfusion. Changes in the slope of the pressure volume curves before and after perfusion (ΔE) were compared between the two groups. Loss of extracellular collagen in DTNB hearts was confirmed by subsequent scanning electron microscopy. After perfusion all hearts were edematous, but the weights of control and DTNB hearts were similar (1.75 ± .16 vs. 1.91 ± .22 grams respectively, mean ± SD). ΔE was significantly greater in C than in DTNB hearts at 2, 5, and 10 mmHg, and showed a similar trend at 25 mmHg. DTNB hearts tended to become more compliant, and C hearts less compliant, at all three levels of pressure.

	ΔE (mmHg/ml)		
mmHg	Control	DTNB	
2	21.4 ± 40.6	-55.4 ± 60.2	p<.02
5	41.6 ± 59.6	-55.0 ± 51.1	p<.02
10	73.2 ± 37.2	-49.4 ± 37.2	p<.02
25	167.4 ± 193.2	-32.7 ± 84.8	NS

Unexpectedly, the effect of destruction of the collagen matrix was greater at lower than at higher diastolic pressures. These data support the hypothesis that the extracellular collagen matrix is an important determinant of left ventricular diastolic function over the normal range of resting pressures.

11:00

AUGMENTATION OF LV RELAXATION IS GREATER FOLLOWING TRIPLE THAN SINGLE EXTRASYSTOLIC CONTRACTION.

Michael Courtois; Carol J Mechem; Philip A Ludbrook, F.A.C.C. Washington Univ., St. Louis, Mo.

We have demonstrated that LV isovolumic relaxation rate following a single short-coupled extrasystolic contraction (ESCx1) is significantly slowed after the first postextrasystolic contraction (PESC-1). Relaxation rate then gradually increases above baseline in the subsequent beats, reaching maximal augmentation following PESC-5. If this augmented relaxation is related to increased levels of myofibrillar calcium following ESC, then additional ESCs should increase the magnitude of augmentation of relaxation. To test this hypothesis we measured LV contractility (peak rate of LV pressure change: +dP/dt) and isovolumic relaxation rate (time required for LV pressure at peak -dP/dt to decay by 1/2: T1/2), in 5 anesthetized dogs at baseline (BL) and in ten consecutive beats following an electrically induced ESCx1, and following a triplet (ESCx3). Time constant of isovolumic relaxation was based on a model of exponential decay with variable asymptote.

		ESCx1			
	BL	PESC-1	PESC-3	PESC-5	PESC-7
+dP/dt	2923±339	4640±256*	3761±334*	3120±267	2760±544
T1/2	20.2±1.8	23.3±2.9*	20.0±2.0	19.1±1.9*	19.3±2.1*
		ESCx3			
	BL	PESC-1	PESC-3	PESC-5	PESC-7
+dP/dt	2820±229	5344±316*#	4275±505*#	3613±372*#	3149±487
T1/2	20.1±1.6	23.3±3.7*	19.8±2.3	18.6±2.1*#	18.3±2.2*#

*p<0.05 versus BL; #p<0.05 versus ESCx1 mean ±SD

These changes in LV contractility and relaxation after ESC remained the same following beta blockade with propranolol. Thus, following ESCx3 both myofibrillar activation and deactivation are augmented above the levels induced by ESCx1. The increase in relaxation rate following ESC may represent the normal physiologic response to augmented levels of contractility mediated by increased levels of myofibrillar calcium. Delineation of the mechanism of this increase in relaxation rate may provide important insights into the processes of normal and abnormal myocardial relaxation.